Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Prior to the present amendment, claims 39-44 were pending in this application and were rejected on various grounds. Claim 44 has been canceled without prejudice and claims 39 has been amended. Support for this amendment can be found on page 210, lines 22 onwards. The rejections to the presently pending claims are respectfully traversed.

Priority

Applicants rely on the Skin Vascular permeability assay (Example 77) to establish patentable utility for the polypeptide PRO326. These results were first disclosed in international application PCT/US98/19437, filed 17 September, 1998 to which priority is claimed in this application. Support is found at Example 77, page 210, lines 22 onwards. Accordingly, the present application is entitled to the effective filing date of 17 September, 1998.

Double Patenting

Claims 39-44 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of co-pending Application No. 09/909088.

As Applicants already have filed a terminal disclaimer in co-pending Application No. 09/904786 which claims antibodies to PRO335 (the Examiner had mistakenly cited US Application No. 09/909088 in the Office Action which recites nucleic acids to PRO335), this rejection is moot.

Thus, Applicants respectfully request that this rejection be withdrawn.

Claim Rejections – 35 USC §101 and 112

Claims 39-44 were rejected under 35 U.S.C. §101 allegedly because the claimed invention was not supported by either a specific, substantial and credible asserted utility or a well established utility.

Utility – Legal Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather**, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the

Proper Application of the Legal Standard

Applicants rely on the skin vascular permeability assay (Example 77, page 210, lines 22 onwards) to establish patentable utility for the polypeptide PRO326. These results were first disclosed in international application PCT/US98/19437, filed 17 September, 1998 to which priority is claimed in this application. Accordingly, the present application is entitled to the effective filing date of 17 September, 1998.

The claims as presently amended recite antibodies that "specifically" bind to the PRO326 polypeptide "wherein said antibody inhibits an immune or inflammatory response."

Example 77 describes a dye-based proinflammatory cell infiltration assay called the skin vascular permeability assay in which PRO326 induces mononuclear cell, eosinophil and PMN infiltration into the site of injection of this peptide/protein into an animal. In the proinflammatory cell infiltration assay, purified or conditioned media containing PRO326 was injected intradermally onto the backs of hairless guinea pigs whereas the Evans blue dye was injected intracardially. Blemishes at the injection sites were measured 1 h and 6 h post injection. Animals were sacrificed at 6 h after injection, the skin at each injection site was biopsied, fixed in formalin and evaluated histopathologically for inflammatory cell infiltration into the skin. Such inflammatory cell infiltration assays are routinely used in the art to evaluate proinflammatory properties of novel compounds (see Rampart et al; enclosed in IDS). For example, in Rampart et al., IL-8 (Interleukin 8) was identified using a neutrophil accumulation assay in rabbit skin (see Methods, page 22) and the findings were correlated with albumin flux and neutrophil dependent edema in skin.

Under proinflammatory conditions, several mechanisms act synergistically to mediate an increase in neutrophil accumulation, plasma extravasation, etc. Such events occur for example, during the acute phase of an inflammatory response to a microbial stimulus or during pathologic conditions like graft rejection, edema, psoriasis, arthritis, tissue injury etc. The enclosed reference, Rampart et al. suggests the involvement of endogenous IL-8 in an acute phase inflammatory response of an animal to a microbial stimulus and further disclosed suggestive data supporting its involvement in psoriasis (see page 24, column 1, last paragraph). Subsequent data

suffering from rheumatoid arthritis, IL-8 is also associated with other inflammatory diseases like asthma, leprosy, psoriasis, inflammatory bowel disease, atherosclerosis, cystic fibrosis, and in various respiratory syndromes. Similarly, a variety of real-life utilities are envisioned for PRO326 based on the proinflammatory cell infiltration assay results disclosed herein. Thus, contrary to the Examiner's assertion, the skin vascular permeability assay is not merely a hypersensitive assay. Instead, results from this assay have been used to identify molecules useful in treating inflammatory diseases and immune diseases. Accordingly, antibodies raised against PRO326 polypeptides can be exploited for their anti-inflammatory properties.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. Indeed, the logic underlying Applicants' assertion that PRO326 may be useful in boosting an immune response is not inconsistent with the general knowledge in the art, and would be considered credible by a person skilled in the art. It is always possible that an invention might fail on its way of development to a commercial product. For example, despite recent advances in rational drug design, a large percentage of drug candidates fails, and never makes it into a drug product. However, the USPTO is not the FDA, the law does not require that a drug product be currently available to the public in order to satisfy the utility requirement.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the 35 U.S.C. §101 rejection.

Claims 39-44 were also rejected under 35 U.S.C. §112, first paragraph since allegedly, the claimed invention was not supported by either a specific, substantial and credible asserted utility.

As discussed above, a specific, substantial and credible utility for PRO326 antibodies have been defined, for example, in inhibiting an inflammatory response. Based on the information disclosed in the specification and that available in the art, one skilled in the art knew how to practice the claimed invention, at the effective priority date of this application, without

Certain Limited-charge cell Culture Microcarriers, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01.

Hence, withdrawal of the 35 U.S.C. §112, first paragraph rejection is requested.

Claim Rejections – 35 USC § 112, second paragraph

Claims 39-44 were rejected under 35 U.S.C. §112, second paragraph, allegedly, as being indefinite since it was not clear how the scope of the two terms "binds" and "specifically binds" differed. Claim 42 was held indefinite because, according to the rejection, an antibody could not be a fragment of itself. Applicants respectfully traverse these rejections.

The art-recognized meaning of "specific" binding is that the antibody binds to a polypeptide of SEQ ID NO:294 and does not significantly cross-react with another antigen. However, solely to simplify issues, and facilitate the prosecution of the present application, claim 44 has been canceled, and claim 39 has been amended to recite specific binding. Accordingly, the present rejections are believed to be moot, and should be withdrawn.

Applicants assert that Claim 42 is not indefinite. The definition of antibody includes antibody fragments and Applicants are entitled to be their own lexicographer; see page 75, line 38 through page 76, line 37. Thus, the rejection to claim 42 must be withdrawn.

Claim Rejections – 35 USC § 102

1. Claims 39-44 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Wu et al., U.S.P.N. 6,046,030 (filing date 12/8/97).

Wu discloses a polypeptide (SEQ ID NO:5) having 51.6 % identity to presently claimed SEQ ID NO:294. Wu does not disclose antibodies to their polypeptide nor that their polypeptide is associated with an immune or inflammatory response. Therefore, all the claim recitations are not taught. Hence, Applicants respectfully request that this rejection be withdrawn.

2. Claims 39-44 were rejected under 35 U.S.C. §102(e) as being anticipated by Wang et al.,

As discussed above, since Applicants are entitled to an effective filing date of 17 September, 1998, Wang is not prior art under 102(e) since its filing date is after the effective priority date.

Hence Applicants respectfully request that this rejection be withdrawn.

Claim Rejections – 35 USC § 103(a)

Claims 39-44 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kawai et al. (6/1/01) or Nagase et al. (5/1/99) or Suzuki et al., (2/1/97) any of the three in view of Sibson et al. (WO 94/01548; filing date 1/20/94). The Examiner alleges that Sibson outlines generally that it is useful to place a desired cDNA sequence into an expression vector, host cell and to raise antibodies to the protein encoded by the cDNA. Thus, the Examiner alleges that it would be obvious to a person of skill in the art to make antibodies to any of the proteins disclosed by Kawai , Nagase or Suzuki according to the teachings of Sibson. Applicants respectfully traverse this rejection.

As discussed above, since Applicants are entitled to an effective filing date of 17 September, 1998, Nagase and Kawai fall as prior art.

Suzuki teaches a polypeptide that has 50.14% identity to the amino acid residues of SEQ ID NO: 294. Suzuki does not teach antibodies to their polypeptide nor that their polypeptide is associated with an immune or inflammatory response.

The claims in the present application are directed to antibodies which specifically bind to a PRO326 polypeptide of SEQ ID NO: 294 and which inhibit an inflammatory response. Suzuki, when taken alone or in combination, provides no suggestion or hint that the P70193 polypeptide would be associated with an inflammatory response, or would otherwise have biological properties similar to those of PRO326. As a result of the unexpected and unanticipated property of the polypeptide to which they bind, the antibodies of the present invention have the unobvious property of being able to inhibit an inflammatory response. Since this property is not disclosed or suggested in Suzuki, or its combination with Sibson, the present rejection is believed to be misplaced, and should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-1618P2C28). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: July 22, 2003

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